Applicant : Wely B. Floriano, Nagarajan Vaidehi,
William A. Goddard, III
Serial No. : 10/010,725
Filed : November 30, 2001
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Attorney's Docket No.: 06618-607002 / CIT 3192-C

REMARKS

Claims 1-6, 8-16, 29, 31 and 36-45 are now pending in the application. Claims 1, 4, 5, 6, 31 and 36 have been amended. Claims 17-28, 30 and 32-35 are cancelled herein. Support for amendments to claims 1 and 31 can be found in the application as originally filed. For example, the recitation of "to a computer processor" finds basis, for example, on page 41, paragraph [0087]. The recitation of "a set of configurations for each ligand by applying a coarse-grained docking algorithm" finds basis, for example, on page 15, paragraph [0032]. The recitation of "energy scoring" finds basis, for example, on page 29, paragraph [0053]. Support for amendments to claim 4 can similarly be found, for example, on page 15, paragraph [0032] and on page 29, paragraph [0053]. Support for amendments to claim 5 can be found, for example, on page 9, paragraph [0011]. Support for amendments to claim 6 can be found, for example, on page 9, paragraph [0012]. No new matter has been added.

A Notice of Appeal to the Board of Patent Appeals and Interferences accompanies this response.

Lack of Written Description, Under 35 U.S.C. § 112, First Paragraph

Claims 1-6, 8-16, 29, 31 and 36-45 are rejected for alleged lack of written description. The Office Action alleges that the claims contain new subject matter which was allegedly not described in the application as originally filed.

Claims 1 and 31

The Office Action alleges that the limitation "the preferred binding conformations being determined by generating and ranking initial conformations for each ligand in the set of ligands at the binding region using docking techniques" does not have support in the application.

Claims 1 and 31 are amended herein to recite:

identifying a plurality of preferred binding conformations for each ligand in the set of ligands in the binding region, the preferred binding conformations being determined by generating a set of configurations for each ligand by applying a coarse-grained docking

algorithm and ranking initial conformations for each ligand in the set of ligands at the binding
region using energy scoring

As discussed above, the amendment finds support in the application. Dependent claims
2-6, 8-16, 29, 31 and 36-43 are also supported by the specification for the reasons discussed
above. Reconsideration and removal of the rejection is requested.

Claim 4

The Office Action alleges that the limitations "scoring a preliminary energy function for
at least some of the initial conformations" and "based at least in part on the preliminary energy
scores" do not have support in the application.

Applicant respectfully submits that as discussed above, amended claim 4 is supported by
the application as filed.

Claims 5, 6 and 36

The Office Action alleges that the limitations "preliminary energy function" and
"preliminary energy score" are not supported by the specification.

Applicant respectfully submits that as discussed above, amended claims 5, 6 and 36 are
supported by the application as filed.

Non-Statutory Subject Matter Under 35 U.S.C. § 101

The Examiner rejects claims 1-6, 8-16, 29, 31 and 36-45 as allegedly directed to non-
statutory algorithm type subject matter. The applicants respectfully disagree.

Applicant submit that claim 1 is amended herein to include the step of

providing to a computer processor, structural information describing the structure of a
protein and each ligand in a set of one or more ligands

Thus, the amended claim contains a physical alteration step wherein the data is providing
to a computer processor. Therefore, claim 1 and the claims dependent thereon are properly
directed to patentable subject matter. Withdrawal of the rejection is requested.

Claim Rejections 35 USC § 102

The Office Action rejects claims 1-6, 8-16, 29, 31 and 36-45 under 35 U.S.C. § 102(a) as
allegedly anticipated by Zou *et al.* It is alleged that Zou *et al.* discloses a method and computer

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program for modeling ligand receptor binding interactions wherein structural information based on solvation effects for the receptors are derived from the crystal structures to identify binding regions. The Office Action further alleges that the reference discloses the use of DOCK to identify 10,000 top force field scoring molecules and then calculate GB calculations to rank these candidates. The reference allegedly discloses 10 best scoring conformations according to free energy calculations. The Office Action concludes that the disclosure of the reference anticipates the instant claims.

Disclosure of Zou *et al*

Zou *et al.* describes the use of the well-known Generalized-Born (GB/SA) model of solvation to estimate ligand binding energies. Zou *et al.* modifies the GB/SA model to account for electrostatic interactions between the ligand and the solvent, introduces a formula to estimate the binding free energy, and then calculates a free energy score for each conformation of one or more ligands. The resulting scores are used to rank ligands or their conformations, and to explore appropriate parameters for the model.

Differences between in the instant claims and the disclosure of Zou

The instant claims require identifying a plurality of preferred binding conformations for each ligand in a set of ligands in the binding region by generating a set of configurations for each ligand by applying a coarse-grained docking algorithm and ranking initial conformations for each ligand in the set of ligands at the binding region using energy scoring. The claimed method further requires optimizing the preferred binding conformations using annealing molecular dynamics, the annealing molecular dynamics including solvation effects; calculating a binding energy for each ligand in the set of ligands in the corresponding optimized preferred binding conformations; and selecting for each ligand in the set of ligands the lowest calculated binding energy in the optimized preferred binding conformations. Thus, the claimed method provides a hierarchical method for modeling ligand-protein binding interactions that performs a coarse grain conformational search with a fast energy scoring. Then, the preferred conformations are optimized using annealing molecular dynamics that include solvation effects.

Zou *et al.* uses one method of conformational search and scoring and retains one conformation. Whereas, the hierarchical method of the instant claims uses efficient coarse-grained docking algorithm to first model initial conformations of ligands and identifies preferred binding conformations by energy scoring. The method then employs computationally intensive and accurate fine-grained methods to further optimize each of the preferred conformations and select the best one – i.e. the one having the lowest energy score.

Thus, Zou *et al.* does not disclose all of the steps of the claimed method, including the steps of by generating a set of configurations for each ligand by applying a coarse-grained docking algorithm, ranking initial conformations for each ligand in the set of ligands at the binding region using energy scoring and then optimizing the preferred binding conformations using annealing molecular dynamics, the annealing molecular dynamics including solvation effects. Since anticipation requires that a reference disclose every element of a claim, Zou *et al.*, which does not disclose the above mentioned steps, does not disclose all of the claimed elements of claim 1 and claims dependent thereon. Therefore, Zou *et al.* does not anticipate claim 1 or any claims dependent thereon, including any of claims 2-6, 8-16, 29, 31 and 36-45 named in this rejection.

* * *

In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested.

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Applicant hereby requests 3 months extension of time. Please apply any charges or credits to deposit account 06-1050.

                                                          Respectfully submitted,

Date:_____4/12/05_____   _____
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